Remarks

Claims 1, 9, and 37-49 were pending in the subject application. By this Amendment, applicants have canceled claims 1, 9, and 37-49 without prejudice or disclaimer, and added new claims 50-59. Accordingly, upon entry of this Amendment, new claims 50-59 will be pending and under examination.

Applicants maintain that the addition of new claims 50-59 do not raise an issue of new matter. Support for new claim 50 can be found *inter alia* in the specification as filed at least on page 3, lines 9-14; page 6, lines 11-15; page 7, lines 12-17 and 23-27; page 19, lines 10-19; page 27, lines 24-28; and in the Experimental Details, page 39, line 18 through page 72, line 21; and in previous claims 1 and 37. Support for new claims 51-59 can be found *inter alia* in the specification as filed at least on page 26, lines 15-16; and on page 27, line 27 through page 28, line 5. Accordingly, applicants respectfully request entry of the Amendment.

Declaration of Dr. George J. Christ

In support of the application, applicants attach hereto as **Exhibit A** (4 pages including Figure) a Declaration of Dr. George J. Christ under 37 C.F.R. §1.132 in which Dr. Christ describes how erectile dysfunction can be treated using two additional potassium channel proteins, the voltage-dependent potassium channel protein Kv1.5 and the calcium-sensitive potassium channel protein SK3. This evidence is in addition to data already described in Example I of the application obtained with the calcium-sensitive potassium channel protein maxi-K and with the metabolically-gated and inward rectifier potassium channel protein K_{ATP}. The data are summarized in Figure 1 of Dr. Christ's Declaration. At the end of paragraph 2 of the Declaration, Dr. Christ states that the data indicate that potassium channel subtypes from all the major potassium channel families (i.e., calcium-activated (maxi-K and SK3), inward rectifier (K_{ATP}), and voltage-

dependent (Kv1.5) potassium channels) are effective in enhancing relaxation of penile smooth muscle.

Information Disclosure Statement

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the references which are listed on the attached form PTO/SB/08A-B (2 pages) (**Exhibit B**) and attached hereto as **Exhibits 1-10**. The references attached as Exhibits 2-9 were cited in a Supplementary Partial European Search Report issued on October 18, 2002 in connection with related European patent application No. 98906170.0. A copy of the Search Report is attached hereto as **Exhibit 11**.

Conclusion

In view of the amendments and remarks made hereinabove, applicants respectfully request passage of the claims to allowance. If there are any minor issues that would prevent allowance, applicants request that the Examiner contact the undersigned attorney.

A check for $840.00 is enclosed to cover (1) the $465.00 fee for a three month extension of time and (2) the $375.00 fee for filing a Request for Continued Examination for a small entity. No other fee is deemed necessary to maintain the pendency of this application. However, if there are unanticipated fees required to maintain the pendency of this application, the PTO is authorized to withdraw those fees from Deposit Account 01-1785. Overcharges may also be credited to Deposit Account 01-1785.

Respectfully submitted,

AMSTER, ROTHSTEIN & EBENSTEIN
Attorneys for Applicant
90 Park Avenue
New York, New York 10016
(212) 697-5995

Dated: New York, New York
May 20, 2003

By: _____
Craig J. Arnold, Registration No.: 34,287
Alan D. Miller, Registration No.: 42,889

#16 add 5/29/03

Docket No. 96700/596

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Jan Geliebter, George J. Christ, Arnold Melman, and Jamil Rehman
Appln. No.	:	09/531,969
Filed	:	March 21, 2000
For	:	GENE THERAPY FOR REGULATING SMOOTH MUSCLE TONE
Art Unit	:	1632
Examiner	:	Peter Paras, Jr.

Declaration of Dr. George J. Christ under 37 C.F.R. §1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Considered 8/15/03 PP

I, George J. Christ, hereby declare as follows:

1. I am a co-inventor of the subject matter claimed in U.S. Patent Application No. 09/531,969. I am currently a Professor in the Department of Urology and the Department of Physiology & Biophysics at Albert Einstein College of Medicine, Bronx, New York. I hold a doctorate degree (Ph.D.).

2. I am familiar with the examination proceedings in this application. In support of the application, I would like to bring to the Examiner's attention evidence of the effectiveness in relaxing penile smooth muscle of two additional potassium channel proteins, the voltage-dependent potassium channel protein Kv1.5 and the calcium-sensitive potassium channel protein SK3. This evidence is in addition to data already described in the application obtained with the calcium-sensitive potassium channel protein maxi-K and with the metabolically-gated and

inward rectifier potassium channel protein K_{ATP}. The experiments with Kv1.5 and SK3 are described in the Example below.

Example

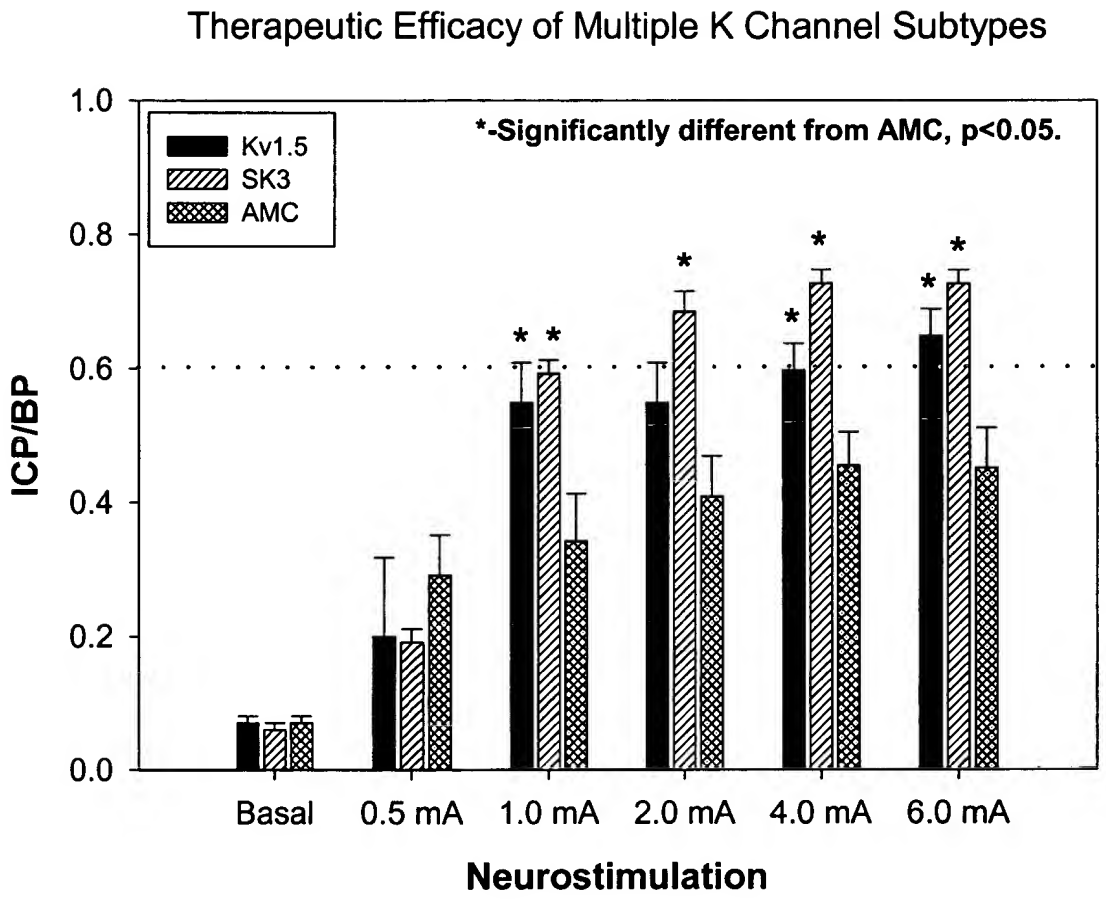
Material and Methods: DNA encoding rat SK3, cloned into plasmid pBF, was obtained from Dr. John Adelman (Kohler M. et al. Science 1996 Sep 20; 273 (5282): 1709-14). DNA encoding human Kv1.5 was cloned by the inventors. The cloned DNA encoding Kv1.5 was inserted into the pVAX expression vector essentially as described in Example I of the current application. 100 µg of pVAX/Kv1.5 (n=5) or pBF/SK3 (n=6) were injected into the corpus cavernosum of retired breeder rats. One week after injection, cavernosometry was performed on all rats. The responses obtained in treated rats were compared to responses obtained with Age-Matched Control (AMC) rats injected with vehicle only (i.e., phosphate buffered saline). The resting intracavernous pressure (ICP), as well as the ICP measured during current stimulation of the cavernous nerve (0.5, 1.0, 2.0, 4.0 and 6.0 mA) were averaged, and statistical comparisons at each level of stimulation were subjected to a One Way ANOVA, with Fischer's Protected Least Significant Difference test used for Post-hoc pair wise comparisons.

Results and Discussion: The results of the experiments are shown in Figure 1. As illustrated in the Figure, the cavernous nerve stimulated ICP responses were significantly greater in gene transfer experiments with both Kv1.5 and SK3 channel subtypes than in Age-Matched Controls (AMC) at most levels of nerve stimulation (i.e., ≥ 1.0 mA). Gene transfer with both Kv1.5 and SK3 channel subtypes produces a ratio of intracavernous pressure to blood pressure commensurate with sufficient relaxation of penile smooth muscle to ensure a penile erection adequate for coitus (intercourse); that is, an ICP/BP ratio >0.6 (dashed horizontal line in Figure 1). The data indicate that potassium channel subtypes from all the major potassium channel families (i.e., calcium-activated (maxi-K and SK3), inward rectifier (K_{ATP}), and voltage-dependent (Kv1.5) potassium channels) are effective in enhancing relaxation of penile smooth muscle.

3. I hereby declare that all statements made herein and of my knowledge are true and that all statements made on information and belief are believed to be true; and I further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 5/12/03

Dr. George J. Christ


Therapeutic Efficacy of Multiple K Channel Subtypes
*-Significantly different from AMC, p<0.05.
Kv1.5
SK3
AMC
ICP/BP
1.0
0.8
0.6
0.4
0.2
0.0
Basal
0.5 mA
1.0 mA
2.0 mA
4.0 mA
6.0 mA
Neurostimulation